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10/541,683

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EXAMINER

WILSON, MICHAEL C

ART UNIT

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1632

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/541,683	Applicant(s) SCHWENK ET AL.	
	Examiner Michael C. Wilson	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-55 is/are pending in the application.
- 4a) Of the above claim(s) 47 and 49-52 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-46, 48 and 53-55 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>7-7-05</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-16 have been canceled. Claims 17-52 are pending.

Election/Restrictions

Applicant's election of Group I, claims 17-46, 48 and 53-55 in the reply filed on 1-28-08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 47 and 49-52 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made without traverse in the reply filed on 1-28-08.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 17-46, 48 and 53-55 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims encompass making transgenic human cells in humans. In particular, "multi-cell organism" in claim 49 and 52-55 encompasses making transgenic humans, which is non-patentable subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

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and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 17-46, 48 and 53-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making transgenic non-human mammals, does not reasonably provide enablement for making any transgenic eukaryotic cell, specifically transgenic fish cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification and the art at the time of filing do not teach Rosa26 genes other than those in mammals. In particular, the specification and the art at the time of filing do not teach how to target the fish Rosa26 gene. Without such guidance, it would have required those of skill undue experimentation to determine how to targeting the Rosa26 gene in fish in particular.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 17-46, 48 and 53-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 17 is indefinite because the term "starting" does not further limit the phrase eukaryotic cells. In addition, the phrase "or is a DNA sequence which can be converted into such gene expression cassette" is unclear. The structure of DNA sequences that can be converted into an expression cassette comprising a gene of interest operably linked to a promoter cannot be envisioned. Next, the

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use of "functional DNA sequence" and "gene expression cassette" together in the claims does not clearly set forth the structure of the DNA introduced into the cells and provides no use later in the claims, thereby making the claim confusing.

Finally, use of "locus" in the claim is indefinite because a "locus" is a position on a gene; the intent of the claim is to introduce DNA into the Rosa26 gene. The term "gene" should be used throughout the claim set instead of "locus."

Claim 18 is indefinite because it is unclear how the targeting vector relates to the "functional DNA sequence" or "gene expression cassette" in claim 17.

Claims 18 and 19 are unclear because they attempt to further limit how the functional DNA sequence is introduced while simultaneously attempting to further limit the structure of the functional DNA sequence, thereby making the claims unclear. Clarification is required.

Claim 19 is indefinite because the phrase "site specific recombinase mediated recombination" is unclear. The metes and bounds of the phrase are not defined in the specification or the art at the time of filing. Therefore, those of skill would not know when they had performed that type of site specific recombination.

The metes and bounds of what applicants consider "derived" in claim 20 are unclear. All eukaryotic cells are from a multi-cellular organism; therefore, it cannot be determined how the claim further limits claim 17.

Claim 28 is indefinite because the metes and bounds of what applicants consider "primary" cannot be determined. The term is not defined in the specification or the art at the time of filing.

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Claim 30 is indefinite because the phrase "pharmaceutically active proteins and peptides" is unclear. It is unclear when a protein or peptide is pharmaceutically active as claimed.

Claim 31 is indefinite because it is unclear if the promoter is "heterologous" to the DNA sequence, the eukaryotic cell or the Rosa26 gene.

The metes and bounds of what applicants consider an "inducible ubiquitous promoter" and "inducible tissue specific promoter" in claim 32 cannot be determined. The structure of such promoters is not defined in the specification or the art at the time of filing.

The metes and bounds of what applicants consider a "CAGGS, hCMV, PGK, FABP, Lck, CamKII, CD19... ..aP2... ..MCK, MyHC, WAP, Col2A, Mx, tet and trex" promoter in claim 33 cannot be determined. The structure of such promoters is not defined in the specification or the art at the time of filing. The abbreviations should be spelled out where necessary or applicants should point to the definition of such abbreviations in the specification or the art at the time of filing.

Claim 34 is indefinite because the claim further optionally limits the "functional DNA sequence" but is actually only further limiting the "gene expression cassette" in the "functional DNA sequence".

Claim 34 is indefinite because "second recombinase recognition sites differing from the first recombinase recognition sites" is unclear because the "first" sites lack antecedent basis and because it is unclear how the first and second sites differ.

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Use of the term "functional" in claims 34 and 35 is confusing because it does not further limit anything, thereby making the claims indefinite.

Claim 35 is indefinite because the phrase "the targeting vector and recombination vector" lacks antecedent basis.

Claim 36 is indefinite because the phrase "the DNA sequences homologous to the Rosa26 locus" lacks antecedent basis. Amending the phrase in claim 36 will require amending the phrase in claim 37 and 38.

Claim 38 is indefinite because the phrase "the transgenic eukaryotic cells" lacks antecedent basis. Claim 38 is indefinite because the term "derived" does not clearly set forth the eukaryotic cells are mouse cells. The claim is also indefinite because the phrase "derived from the 5' and 3' flanking arm of the mouse Rosa26 locus" is unclear and does not clearly set forth the structure of the homology arms or that the Rosa26 gene is a mouse Rosa26 gene.

Claim 39 is indefinite because the term "respectively" is unclear.

Claim 40 is indefinite because the term "derived" does not clearly set forth the eukaryotic cells are mouse cells.

Claim 42 is indefinite because the phrase "two mutually incompatible first RRSs" is unclear. It cannot be envisioned how RRSs are mutually incompatible. Furthermore, use of "two" and "first" together to describe the RRSs makes the claim unclear.

The phrase "starting cells" in claim 42 lacks antecedent basis. Claim 42 is also indefinite because it is unclear how the "acceptor DNA" correlates to the

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"functional DNA sequence", "gene expression cassette" or the "recombination vector" in the parent claim.

The phrase "introducing into the therewith obtained cell" in claim 42 is actually part of step a2; steps a2 and a3 should be method steps, not DNA. The phrase "the same two mutually incompatible first RRSs" in claim 42 does not make sense; the structure of the RRSs. The phrase "by utilizing a recomaintion vector as defined in claim 19" is unclear because it cannot be determined how the phrase further limits the step of introducing or the structure of the vector. The phrase "the recombinase" in step a3 lacks antecedent basis.

Claim 42 is indefinite because the steps of the method should be clearly set forth as steps a, b and c.

Claim 45 is indefinite because it is unclear what applicants consider an "inactive" positive selection marker.

Claim 46 is indefinite because the steps selected from the group should be a) and b). If applicants are attempting to indicate the steps in claim 46 occur after the step in claim 17, clarification is required. Claim 46 is indefinite because step "b" should clearly indicate the eukaryotic cells having the "desired functional DNA sequence integrated into the Rosa26 locus" are isolated; the phrase "preferably the ES cells" makes the method step unclear. If applicants intend to further limit the cells to ES cells, clarification is required.

Claim 46 is indefinite because the "desired functional DNA sequence" is unclear; the phrase is not defined in the specification or the art at the time of filing and does not further limit the structure of the DNA sequence. If applicants are

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attempting to indicate cells having the DNA sequence integrated into the Rosa26 gene are isolated, clarification is required.

Claim 46 is indefinite because the phrase "the integrated functional DNA sequence" lacks antecedent basis.

Claim 46 is indefinite because the step of "isolating ES cells having the desired" should be a separate step and because "desired" is unclear and because the previous steps are not limited to ES cells.

It cannot be determined how the process of claim 17 further limits the "eukaryotic cell having a modified Rosa26 locus" as in claim 48.

Claim 53 is indefinite because it does not set forth any steps for "studying gene function."

Claims 54 and 55 are indefinite because they do not set forth any steps for "drug development."

Claim 55 is indefinite because it does not set forth any steps for how the biological entities are disease model animals. The scope of "eukaryotic cell, transgenic multi-cell organism or transgenic non-human mammal" does not have the same scope as "disease model animal."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 17-25, 28-32, 34-38, 42-46, 48 and 53-55 are rejected under 35 U.S.C. 102(b) as being anticipated by Soriano (WO99/53017).

Soriano made a Rosa26 transgenic mouse by introducing a DNA cassette comprising a LacZ gene flanked by loxP sites into the Rosa26 locus of a mouse ES cell and implanting the ES cell into a mouse blastocyst. The LacZ gene was under the control of the mouse Rosa26 promoter (Example 1, pg 30). Soriano also taught making a Rosa26Cre transgenic mouse (Example 2, pg 41) by introducing a construct into ES cells, the construct comprising a deleter cassette comprising a recombinase gene operably linked to an upstream splice acceptor (SA and a downstream polyA sequence with a positive selection cassette comprising a PGK promoter, the neo gene and a polyadenylation sequence (pg 7, lines 2-10). The construct was inserted into the targeting vector comprising homology arms for the Rosa26 gene and a diphtheria toxin gene for negative selection (pg 7, line 9-10; pg 7, line 1-2). Soriano also made a transgenic mouse by introducing a targeting vector into mouse ES cells, the vector comprising a reporter cassette comprising a splice acceptor operably linked to stuffer DNA flanked by two loxP sites (pg 7, lines 10-16); the stuffer DNA comprised a PGK promoter, the neo gene and four polyA sites (pg 44, Example 3). The methods of Soriano are those claimed.

Conclusion

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The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Soriano (US Patent 6,461,864)

Soriano (Nature genetics, Jan. 1999, Vol. 21, pg 70-71)

Kuhn (WO02/38613)

Economides (WO 02098217)

Economides (WO03/020743)

Dacquin (Develop. Dynamics, June 2002, Vol. 224, No. 2, pg 245-251)

Moses (Genesis: the journal of genetics and development, Dec. 2001, Vol. 31, No. 4, pg 176-180)

Schwenk (EP 1439234 A1)

No claim is allowed.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/
Patent Examiner